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EXAMINER	
FINN, MEGHAN R	
ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTO.e-Office.rdg@boehringer-ingelheim.com

Office Action Summary	Application No.	Applicant(s)	
	10/825,580	KOHLRAUSCH, ANJA	
	Examiner	Art Unit	
	MEGHAN FINN	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,9 and 12-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-5, 9, 12-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant submitted remarks on July 14, 2008 in response to the final office action mailed April 28, 2008. In light of applicant's invoking 35 USC 103(c), the finality of the previous Office Action is hereby withdrawn and new grounds of rejection set forth herein. In light of the reopening of prosecution, the Notice of Appeal filed 7/14/2009 is deemed moot.

Applicants' arguments, filed July 14, 2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29

USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 4-5, 9, and 12-20 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8-9 of U.S. Patent No. 6,737,432 in view of Lacourciere et al. (Comparison of fixed-dose combination of 40mg telmisartan plus 12.5mg hydrochlorothiazide with 40mg telmisartan in the control of mild to moderate hypertension, already of record in the previous office action mailed April 28, 2009).

In claims 8-9 of patent 6,737,432, Donsbach et al. claim a pharmaceutical composition comprising crystalline telmisartan sodium salt and a pharmaceutically acceptable carrier. The carriers listed in the specification include many of the same carriers claimed by applicant in the instant claims 2, 9, and 18-20 including mannitol

(columns 9-10, tablets 1-3). The open language of comprising in claims 8 and 9 can include other components and it was known in the art that to combine telmisartan and hydrochlorothiazide as taught by Lacourciere et al. who teaches the dosages claimed by applicant and it would have been obvious to one of ordinary skill in the art at the time of the invention that the crystalline form of telmisartan sodium claimed in 6,737,432 could be combined with hydrochlorothiazide and administered in the same manner as taught by Lacourciere et al. Thus claims 1-2, 4-5, 9, and 12-20 are unpatentable over claims 8-9 of US patent 6,737,432 in view of Lacourciere et al.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-5, 9, and 12-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In claim 1, and all the independent claims, applicant claims "a crystalline telmisartan sodium salt" but applicant does not have written support for all crystalline forms of telmisartan. In the specification applicant has described one crystalline form (page 3 of specification) with a specific melting point and spectroscopic data (page 4).

One of skill in the art would expect there to be more than one crystalline form of telmisartan as evidenced by Vippagunta et al. (Advanced Drug Delivery Reviews, 2001, vol. 48, pages 3-2) who teaches that most organic and inorganic compounds of pharmaceutical relevance can exist in one or more crystalline forms (page 4, paragraph 1) and that there may be many polymorphs of the same compound that have different physico-chemical properties (page 4, paragraph 2) and that these differences have an important effect on the solubility and absorption of the active drug (page 4, paragraph 4). Dinnebier et al. (Journal of Pharmaceutical Sciences, 2000, Vol. 89 (11), pages 1465-1479) teaches three different crystalline structures for telmisartan, which appear to be different crystalline structures than the one example provided by Applicants. Applicant has provided no direction toward what possible crystalline structures may be out there and has not demonstrated that they had possession of these other crystalline forms at the time of the invention. Thus the specification does not have written description for any beyond the specific one characterized by the physical properties described on page 4 of the specification. Thus claims 1-2, 4-5, 9, and 12-20 lack written description of the invention.

Claims 1-2, 4-5, 9, and 12-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific crystalline form with a melting point of 245°C and the x-ray diffraction data of Table 1 (page 4 of specification) does not reasonably provide enablement for the other crystalline forms encompassed by a crystalline telmisartan sodium salt. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicant has not shown how to make other crystalline forms of telmisartan sodium other than that shown on pages 3-4 of the specification. One of skill in the art would not be able to make the other crystalline forms encompassed by the claims based on the information provided by applicant.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The amount of experimentation necessary would be undue (1) because of the lack of direction towards finding any other crystalline forms besides the specific one detailed on pages 3-4 of the specification (2). The examples are solely directed towards that one form (3) and the nature of the invention is that the claims encompass any crystalline form many of which had different physical properties (4). The state of the prior art is such that there are only a few crystalline forms (those taught by Dinnebier et al.) known and there is not enough information to allow one of skill in the art to make

other unknown crystalline forms that are encompassed by the claims (5). The skill of those in the art is high (6) but the unpredictability of discovering new crystalline forms is very high (7). The breadth of the claims is large due to the unknown number of possible crystalline forms of telmisartan (8).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 4-5, 9, and 12-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lacourciere et al. (Comparison of fixed-dose combination of 40mg telmisartan plus 12.5mg hydrochlorothiazide with 40mg telmisartan in the control of mild

to moderate hypertension) in view of Donsbach et al. (US 2003/0130331 A1), each already of record on pages 3-6 of the previous office action dated April 28, 2009 the reasons of which are hereby incorporated by reference.

In claim 1, applicant claims a pharmaceutical composition comprising a crystalline telmisartan sodium salt and hydrochlorothiazide. In claim 2 applicant claims that the composition further comprises an excipient such as mannitol. In claim 9 applicant claims the combination of a crystalline telmisartan sodium salt and hydrochlorothiazide and mannitol. Lacourciere et al. teaches a combination of telmisartan and hydrochlorothiazide to treat hypertension(abstract). They do not teach the crystalline form, however Donsbach et al. teaches the same crystalline telmisartan sodium salt as claimed by applicant (page 1, [0011] and claims 1-2, 8-9), and the same one which applicant has described in their specification (pages 3-4). They further teach that this is a new stable crystalline form of telmisartan (page 1, [0010]). They also teach mannitol as an excipient with the crystalline telmisartan sodium salt (pages 5-6, tablets 1-3) It would have been obvious to one of ordinary skill in the art at the time of the invention to use the new more stable formulation of telmisartan sodium in place of the telmisartan of Lacourciere et al. and claims 1-2, and 9 are unpatentable over Lacourciere et al. in view of Donsbach et al.

In claims 4-5 and 12-13 applicant claims that the amount of hydrochlorothiazide of claims 1 or 9 is between 10-15mg (claims 4 and 12) or between 12-13mg (claims 5 and 13). Lacourciere et al. teaches 12.5mg of hydrochlorothiazide (abstract) and thus claims 4-5 and 12-13 are unpatentable over Lacourciere et al. in view of Donsbach et al.

In claims 14-17, applicant clams various amounts of crystalline telmisartan sodium from 60-90mg (claim 14) to 80-85mg (claim 15) to 30-60mg (claim 16) to 40-45mg (claim 17). Lacourciere et al. teaches 40mg as their preferred dosage of telmisartan (abstract) however they also teach a dose-response effect up to 80mg telmisartan (page 2 of full text section of the reference, 4th page of enclosed document, under the Introduction section, 3rd paragraph) and thus it would have been obvious to one of ordinary skill in the art at the time of the invention that dosages as high as 80mg were known in the art and within the limits or routine optimization for a particular patient depending on need and effectiveness. Thus claims 14-17 are unpatentable over Lacourciere et al. in view of Donsbach et al.

In claim 18, applicant claims a composition of a crystalline telmisartan sodium salt, hydrochlorothiazide, sorbitol, and magnesium stearate, compressed directly into tablets. As discussed above, Lacourciere et al. teaches the combination of a crystalline telmisartan sodium salt and hydrochlorothiazide, and Donsbach et al. teaches the crystalline form of telmisartan they also teach magnesium stearate as a preferred excipient and specifically teach forming tablets with the composition (pages 5-6, tablets 1-3) and while they do not specifically teach sorbitol it would have been obvious to one of ordinary skill in the art at the time of the invention to use sorbitol to sweeten the composition as desired for better taste to applicant. Thus claim 18 is unpatentable over Lacourciere et al. in view of Donsbach et al.

In claim 19, applicant claims a composition comprising compressed dry granules of a crystalline telmisartan sodium salt, mannitol, magnesium stearate, and

hydroxypropylcellulose with a mixture of hydrochlorothiazide, mannitol, microcrystalline cellulose, and glycol starch. As discussed above, Donsbach et al. teaches a crystalline telmisartan sodium salt, mannitol, magnesium stearate, and while they do not teach hydroxypropylcellulose they do teach lubricants (page 5, [0061]) and hydroxypropylcellulose is well known in the art as a lubricant and would be well within the limits of routine optimization for one of ordinary skill in the art to add the appropriate amount to the composition of Lacourciere et al. With regards to hydrochlorothiazide, Lacourciere et al. does not specify what formulation of hydrochlorothiazide is used the excipients mannitol, microcrystalline cellulose, and sodium glycol starch are all well known in the art and within the limits of routine optimization for developing a tablet containing hydrochlorothiazide. Thus claim 19 is unpatentable over Lacourciere et al. in view of Donsbach et al.

In claim 20, applicant claims a comprising a crystalline telmisartan sodium salt and one or more excipients including carboxymethylcellulose or water. Donsbach et al. teaches carboxymethylcellulose as an excipient used with crystalline telmisartan sodium salt (page 5, [0061]) and any composition upon exposure to the air will contain at least some portion of water and thus the compositions of both Donsbach et al. and Lacourciere would also contain water in some concentration and thus claim 20 is also unpatentable over Lacourciere et al. in view of Donsbach et al.

Claims 1-2, 4-5, 9, and 12-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hauel et al. (US 5,591,762) in view of Dinnebier et al. (Journal of Pharmaceutical Sciences, 2000, Vol. 89 (11), pages 1465-1479), in further view of Vippagunta et al. (Advanced Drug Delivery Reviews, 2001, vol. 48, pages 3-2).

In claim 1, applicant claims a pharmaceutical composition comprising a crystalline telmisartan sodium salt and hydrochlorothiazide. In claim 2 applicant claims that the composition further comprises an excipient such as magnesium stearate. In claim 9 applicant claims the combination of a crystalline telmisartan sodium salt and hydrochlorothiazide and mannitol. Hauel et al. teaches telmisartan as their preferred compound (abstract) and they teach combining that compound with additional active substances such as hydrochlorothiazide (column 57, lines 3-15). They also teach combining the active ingredient (telmisartan) with magnesium stearate (column 133, example 230). They also teach use of bases such as sodium hydroxide to form the sodium salt of the compounds (column 51, lines 5-14). They do not teach the crystalline form of telmisartan, however Dinnebier et al. teaches that there are three crystalline structures of telmisartan (abstract) and teaches that polymorphism can affect the chemical, biological and pharmaceutical properties of a drug (page 1465, paragraph 1). Vippagunta et al. teaches that those differences in physical properties can have an important effect on the processing of drug substances from drug products and the differences in solubility can have an effect on the absorption of the active drug from its dosage form (page 4, paragraph 4). It would have been obvious to one of ordinary skill in the art at the time of the invention that the crystalline form of telmisartan was known,

as well as the different physical properties of such crystalline forms and it would have been obvious to use a crystalline form such as those taught by Dinnebier et al. in the formulation of Hauel et al. Thus claims 1,-2, and 9 are unpatentable over Hauel et al. in view of Dinnebier et al. in further view of Vippagunta et al.

In claims 4-5 and 12-13 applicant claims that the amount of hydrochlorothiazide of claims 1 or 9 is between 10-15mg (claims 4 and 12) or between 12-13mg (claims 5 and 13). Hauel et al. teaches 15-200mg of hydrochlorothiazide which is within the range of claims 4 and 12, and is close enough to the claimed 12-13mg that it is within the limits of routine optimization. Furthermore, dosages as low as 12.5 were known in the art at the time of the invention as discussed above. Thus claims 4-5, and 12-13 are unpatentable over Hauel et al. in view of Dinnebier et al. in further view of Vippagunta et al.

In claims 14-17, applicant clams various amounts of crystalline telmisartan sodium from 60-90mg (claim 14) to 80-85mg (claim 15) to 30-60mg (claim 16) to 40-45mg (claim 17). Hauel et al. teaches 50mg and 100mg of the active ingredient (column 133, examples 230 and 232). Given that the preparation of those examples includes a variety of compounds of which telmisartan is an exemplary compound it would have been obvious to one of ordinary skill in the art at the time of the invention that dosages such as 80mg and 45mg are within the limits of routine optimization for that specific drug and as discussed above were known in the art as evidenced by Lacourciere et al. Thus claims 14-17 are unpatentable over Hauel et al. in view of Dinnebier et al. in further view of Vippagunta et al.

In claim 18, applicant claims a composition of a crystalline telmisartan sodium salt, hydrochlorothiazide, sorbitol, and magnesium stearate, compressed directly into tablets. Hauel et al. teach their telmisartan formulation to contain magnesium stearate (column 133, example 230) as well as sorbitol (column 133, example 232) as well as teaching tablets (example 230). Thus claim 18 is also unpatentable over Hauel et al. in view of Dinnebier et al. in further view of Vippagunta et al.

In claim 19, applicant claims a composition comprising compressed dry granules of a crystalline telmisartan sodium salt, mannitol, magnesium stearate, and hydroxypropylcellulose with a mixture of hydrochlorothiazide, mannitol, microcrystalline cellulose, and glycol starch. Hauel et al. teaches telmisartan, sodium salts, and magnesium stearate as discussed above. They further teach hydrochlorothiazide, microcrystalline cellulose as discussed above. They do not teach hydroxypropylcellulose or glycol starch, however these are commonly used excipients that are well within the limits of routine optimization for one of ordinary skill in the art upon formulating a desired pharmaceutical Composition. Thus claim 19 is also unpatentable over Hauel et al. in view of Dinnebier et al. in further view of Vippagunta et al.

In claim 20, applicant claims a comprising a crystalline telmisartan sodium salt and one or more excipients including microcrystalline cellulose or water. Hauel et al. teach the active substance with microcrystalline cellulose (column 133, example 230) as well as with water (column 133, example 232) and thus claim 20 is also unpatentable over Hauel et al. in view of Dinnebier et al. in further view of Vippagunta et al.

Conclusion

No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meghan Finn whose telephone number is (571) 270-3281. The examiner can normally be reached on 7:30am-5pm Mon-Thu, 7:30am-4pm Friday (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Meghan Finn

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614